REMARKS

Claims 1-3, 21, and 22 are pending. No claims have been allowed.

The Claims were amended as suggested by the Examiner. The specification was also amended as suggested by the Examiner. The specification was also amended as follows.

The specification was amended at line 16 on page 13 to replace "U.S. Serial No. 09/156,954, filed September 18, 1998" with "U.S. Patent 6,153,394 to Mansfield et al." which is the issued patent for the '954 application.

The specification was amended at line 34 on page 29 to replace "U.S. Provisional Application Serial No. 60/120,831, filed on February 19,1999" with "U.S. Serial No. 09/506,630, filed February 18, 2000" which is the corresponding regular application for the provisional application.

1. The specification was objected for containing various informalities. The informalities have been corrected in the manner suggested by the Examiner. In particular, lines 5-10 on page 1 of the specification relating to federal sponsorship has been cancelled and the phrase "and drawings" on page 11, line has been cancelled.

2. Claims 1-3, 22, and 23 have been rejected under 35 U.S.C. § 112, second paragraph.

Claims 1 and 22 have been amended as suggested by the Examiner to render the claims clear and definite. The claims were also amended to call for antibodies against the 16 (±4) and 30 (±4) kDa antigens and not to particular epitopes of the antigens. In addition, the term "unique" was cancelled and the claims amended to refer to the antigens as "specific to" *Sarcocystis neurona*.

The term "unique" had been intended to indicate that the antigens are specific to *Sarcocystis neurona* and are not antigens common to other *Sarcocystis* spp. The applicants teach in commonly owned U.S. Serial No. 09/156,954 (filed September 18, 1998), which is now U.S. Patent 6,153,394, and commonly owned U.S. Provisional Serial No. 60/120,831 (filed February 19, 1999), which is now U.S. Serial No. 09/506,630 (filed February 18, 2000), that particular *Sarcocystis neurona* antigens have epitopes that cross-react with anti-sera against other *Sarcocystis* spp.[1] Because horse antisera commonly includes antisera against other *Sarcocystis*

---

[1] Both the '954 application and thus the '394 patent and the '831 provisional and thus the '630 application were incorporated by reference in the instant application.

spp., identification of *Sarcocystis neurona* specific antigens can be problematic.

To avoid identifying antigens not specific to *Sarcocystis neurona*, the applicants teach a novel immunoassay in the '394 patent which is designed to identify antigens specific to *Sarcocystis neurona*. Using the immunoassy, the applicants identified a 16 (±4) and a 30 (±4) kDa antigen both of which are specific to *Sarcocystis neurona*. Therefore, the particular 16 (±4) and 30 (±4) kDa antigens in the claims are unique to or specific to *Sarcocystis neurona*.

It is believed that the presently amended claims, which recite that the antibodies are specific to the 16 (±4) and 30 (±4) kDa antigens of *Sarcocystis neurona*, adequately describe the antibodies and sets forth the inventive concept. Therefore, to further identify the amino acid sequences that the antibodies recognize is not believed to be necessary.

Claim 21 was amended to make clear that the equid is inoculated with the antibodies to provide the passive protection to the equid.

In light of the amendments, it is believed that Claims 1-3, 22, and 23 are no longer vague and indefinite. Reconsideration of the rejection is requested.

3. Claims 1-3, 22, and 23 have been rejected under 35 U.S.C. § 112, first paragraph.

In essence the rejection argues that the claims directed to vaccines comprising antibodies against at least one epitope of the 16 (±4) and 30 (±4) kDa antigens are not enabled because the specification does not teach by specific example whether the claimed vaccine would work. The rejection relies on Liang for support.

Liang teaches that antisera from *Sarcocystis neurona* infected horses contain antibodies against 14 kDa and 16 kDa antigens which are neutralizing and antibodies against a 30 kDa antigen which are *not* neutralizing. Liang had shown that result by neutralization tests which measured shizonts that appeared after incubating merozoites with the antisera. The results showed that antibodies in the antisera against the 16 kDa antigen caused the number of shizonts to decrease whereas antibodies against the 30 kDa antigen did not. While the results indicated that antibodies against the 30 kDa antigen were not neutralizing *in vitro*, the results did not indicate what effect antibodies against the 30 kDa antigen would have *in vivo*. However, Liang states "The high rate of exposure to *Sarcocystis neurona* and the relatively low incidence of clinical EPM indicate that most horses

develop effective immunity that may prevent entry into the central nervous system . . . ." (page 1834, right col.) Consistent with that statement, Liang and the applicants show that antisera from horses with EPM have antibodies against several *Sarcocystis neurona* antigens, in particular the 16 and 30 kDa antigens. Since most horses with EPM have antibodies against the 16 and 30 kDa antigens but few of these horses have clinical EPM, the 16 and 30 kDa antibodies may have a role in preventing entry of *Sarcocystis neurona* into the central nervous system, i.e., providing passive protection against clinical EPM. Liang teaches that antibodies against the 30 kDa antigen are recognized as specific (page 1837, left col., first para.), which implies that the 30 kDa antigen is common to *Sarcocystis* spp. and not unique to *Sarcocystis neurona*. However, the applicants teach that antisera from horses infected with *Sarcocystis neurona* contains antibodies specific for the 30 kDa antigen of *Sarcocystis neurona* which indicates that the 30 kDa antigen is specific to *Sarcocystis neurona*. Therefore, because horses with EPM but without clinical EPM have antibodies against the 16 and 30 kDa antigens and the applicants teach that the 30 kDa antigen is specific to *Sarcocystis neurona*, there is a nexus between the 16 and 30 kDa-specific antibodies and a functional vaccine comprising the antibodies which

makes it reasonable for one skilled in the art to believe that the applicants' claimed vaccine comprising antibodies against the 16 (±4) and 30 (±4) kDa antigens would inhibit *Sarcocystis neurona* from invading neural tissue.

Liang provides further support for the nexus between the 16 (±4) and 30 (±4) kDa-specific antibodies and a functional vaccine comprising the antibodies as claimed by the applicants. Liang (page 1836, left col. and Figure 3) teaches that the 14 and 16 kDa antigens are effective surface antigens. Because surface antigens are generally important in the function or life-cycle of the organism, it is reasonable to believe that blocking the activity of the antigens by binding with antibodies would interrupt the function or life-cycle of the *Sarcocystis neurona*. Therefore, a vaccine that contains antibodies against the 16 (±4) and 30 (±4) kDa antigens would be expected to provide sufficient antibodies to a vaccinated horse to inhibit invasion of neural tissue by *Sarcocystis neurona*.

While Liang teaches that a "10-minute exposure to antiserum was required to yield a significant reduction in parasite production" and that "may partially explain why protective antibodies to some apicomplexan parasites are effective in vitro but not in vivo" (page 1837, left col.,third para.), Liang

suggests that the reason is that "newly released parasites are exposed to serum for a shorter time in vivo, and the access of neutralization-sensitive epitopes to antibody may be limited" and that "[m]erozoites in vivo may move more directly from cell to cell" (page 1837, left col.,third para.). While the statements may suggest that humoral responses to *Sarcocystis neurona* may be of limited efficacy in inhibiting parasite production, the statements do not suggest that humoral responses would have no efficacy against disease caused by *Sarcocystis neurona*. In fact, Liang suggests that antibodies against the 14 and 16 kDa antigens may be efficacious against disease caused by *Sarcocystis neurona* because Liang also teaches that "humoral responses may explain why many horses with EPM do not have clinical EPM by teaching that "in the case of EPM, disease occurs only after the merozoite passes through the vascular endothelium of the blood-brain barrier into the central nervous system, and so humoral responses may play an essential role in blocking this migration" (page 1837, left col.,third para.) particularly since "specific cytotoxic T-cells are ineffective in attacking merozoites migrating to the central nervous system in the bloodstream" (page 1837, left col., third para.).

In light of the above, it is clear that what

Liang is teaching is that antibodies against the 14 and 16 kDa antigens would be expected to be efficacious at inhibiting disease caused by *Sarcocystis neurona*, i.e., clinical EPM, even if the antibodies may not be efficacious at preventing parasite production. The applicants' claimed vaccine which comprises antibodies against the 16 (±4) and 30 (±4) kDa antigens is consistent with the teachings of Liang. Therefore, the applicants' disclosure is believed to be enabling for a vaccine that provides passive immunity to *Sarcocystis neurona* comprising antibodies against the 16 (±4) kDa and 30 (±4) kDa antigens as presently claimed in Claims 1-3, 21, and 22. Reconsideration is requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attachment is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

In view of the above, it is believed that Claims 1-3, 21, and 22 are in proper form for allowance. Notice of allowance is requested.

Respectfully,

Ian C. McLeod
Registration No. 20,931

MCLEOD & MOYNE, P.C.
2190 Commons Parkway
Okemos, MI 48864
(517) 347-4100
FAX (517) 347-4103

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at page 1, line 5, and ending at page 1,line 8, was amended as follows.

[

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

None.]

The paragraph beginning at page 11,line 1, was amended as follows.

These and other objects of the present invention will become increasingly apparent by reference to the following embodiments [and drawings].

Paragraph beginning at page 13, line 1, was amended as follows.

The present invention provides a vaccine that protects equids against *Sarcocystis neurona*. In a preferred embodiment, the vaccine consists of a 16 (±4) kDa antigen and/or 30 (±4) kDa antigen in a subunit vaccine. Preferably, the 16 (±4) kDa antigen and/or 30

(±4) kDa antigen are produced in a recombinant bacterium or eukaryote expression vector which produces the proteins which are then isolated to make the vaccine. In another embodiment of the vaccine, the vaccine is a DNA vaccine that comprises a recombinant DNA molecule, preferably in a plasmid, that comprises DNA encoding all or part of the 16 (±4) kDa antigen and/or 30 (±4) kDa antigen. In another embodiment of the vaccine, the recombinant DNA is inserted into a virus vector to provide a live vaccine which is a recombinant DNA virus. In U.S. [Serial No. 09/156,954, filed on September 18, 1998] Patent 6,153,394 to Mansfield *et al.*, which is hereby incorporated herein by reference, it was disclosed that *Sarcocystis neurona* possesses two unique antigens, a 16 (±4) antigen and a 30 (±4) kDa antigen. These antigens do not react with antibodies from other *Sarcocystis* spp. Thus, these antigens are useful for producing vaccines that protect equids against *Sarcocystis neurona*.

The paragraph beginning at page 29, line 13, was amended as follows.

Therefore, in a Western blot embodiment consisting of *Sarcocystis neurona* antigens resolved by gel electrophoresis, a biological sample from a

vaccinated equid would contain antibodies that bind only with the 16 (±4) antigen and 30 (±4) kDa antigen whereas a sample from an equid infected with, or exposed to, *Sarcocystis neurona* would contain antibodies that bind with additional *Sarcocystis neurona* antigens. The equine antibodies that are bound are identified by treating the blot with labeled antibodies against equine antibodies. Preferably, the label is selected from the group consisting of alkaline phosphatase, horseradish peroxidase, fluorescent compounds, luminescent compounds, colloidal gold, and magnetic particles. Methods for preparing and analyzing Western blots are well known in the art. In a preferred embodiment, the Western blot is pretreated with non-equine antibodies against a *Sarcocystis* sp. other than *Sarcocystis neurona* wherein the pretreatment prevents binding of equine antibodies to those antigens common to all *Sarcocystis* spp. which can be present in the sample. This method is disclosed in [Provisional Patent Application Serial No. 60/120,831, filed on February 19, 1999] U.S. Serial No. 09/506,630, filed February 18, 2000, which is hereby incorporated herein by reference.

In the Claims:

Claims 1 and 21 were amended as follows.

-1- (Amended)

A vaccine for providing passive [immunity] protection to an individual infected with *Sarcocystis neurona* [infection] comprising antibodies which are against [at least one epitope of a unique] a 16 [(±4)] ±4 kDa [or] antigen and a 30 [(±4)] ±4 kDa antigen both of which are specific to [of] *Sarcocystis neurona*.

-21- (Amended)

A method for providing passive [immunity] protection to an equid infected with [a] *Sarcocystis neurona* [infection in an equid] comprising:

(a) providing antibodies against [at least one epitope of] a 16 [(±4)] ±4 kDa antigen and[/or] a 30 [(±4)] ±4 kDa antigen [of] both of which are specific to *Sarcocystis neurona* wherein the antibodies are selected from the group consisting of polyclonal antibodies and monoclonal antibodies; and

(b) inoculating the equid with the antibodies to provide the passive protection to the equid.